

Remarks

Claims 1-20 were pending in the subject application. By this Amendment, Applicants have amended claims 1, 13, 17, and 18 and canceled claims 2 and 3. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1 and 4-20 are currently before the Patent Office. Favorable consideration of the pending claims is respectfully requested.

The claims have been amended to refer to compositions comprising a tissue glue and a radiotherapeutic agent whose therapeutic effect is mediated locally while immobilized in the glue. Thus, rather than being slowly released from within the tissue glue, the agent remains immobilized during the course of the primary therapeutic activity. The claimed compositions are not, therefore, controlled release compositions such as those described in the prior art but are compositions wherein the immobilized agent is not released. As explained at page 9, lines 10-13, of the subject specification, because the radiotherapeutic agent is incorporated into a particle which cannot diffuse through the tissue glue (*i.e.*, it is immobilized), the use of such a tissue glue composition prevents leakage of the agent around the site of application. The agent therefore has a localized therapeutic effect in the area of the tissue glue.

The Examiner has previously rejected the claims under 35 USC §103 in an Office Action dated December 12, 2000 in parent application Serial No. 08/776,737 as obvious based on the teaching of Sierra *et al.* in combination with that of Bhargava *et al.* or Matsueda *et al.* However, Applicants respectfully assert that in the cited references, release of the drug or particle from the tissue glue matrix is necessary in order to achieve the therapeutic effect. In particular, in the Sierra *et al.* reference, the purpose of a tissue glue is not to immobilize, but rather is to slow or impede the diffusion of a drug, such as an antibiotic, so that it is available locally for a longer period of time.

The cited references do not teach or contemplate the use of tissue glues for the administration of particles which require immobilization during the full course of the primary therapeutic activity. As explained above, Applicants' claimed methods are not methods for controlled release as in the prior art but are methods which do not require the release of the immobilized particles. Accordingly, Applicants respectfully assert that the compositions and methods now claimed are not taught or suggested by the references cited by the Examiner and, therefore, the claimed invention is not obvious over the references.

It should be understood that these amendments have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in any of the rejections set forth in the Office Actions in parent application Serial No. 08/776,737.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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DRP/sl

Attachment: Marked-Up Version of Amended Claims

Marked-Up Version of Amended Claims

Claim 1 (amended):

1. A composition comprising a tissue glue and, [retained] immobilized in the glue, in particulate form, a radiotherapeutic agent or an agent convertible to a radiotherapeutic, whose therapeutic effect is mediated locally, [on degradation of the glue] when immobilized in the glue.

Claim 13 (amended):

13. A composition according to claim 1, further comprising an antibody, [a particulate radionuclide] and wherein the tissue glue is a fibrinogen tissue glue.

Claim 17 (amended):

17. A method for making a radiotherapeutic composition [comprising an antibody, a particulate radionuclide and a fibrinogen tissue glue] according to claim 13, which comprises:

- (a) preparing a particulate radionuclide; and
- (b) mixing the particulate radionuclide with the fibrinogen tissue glue and the antibody.

Claim 18 (amended):

18. A method of using a radiotherapeutic composition [comprising an antibody, a particulate radionuclide and a fibrinogen tissue glue] according to claim 13, which comprises applying the composition directly to tumor tissue.